## ENVIRONMENTAL PROTECTION AGENCY

[FRL-5306-2]

## Proposed Guidelines for Neurotoxicity Risk Assessment

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Proposed guidelines for Neurotoxicity Risk Assessment and request for comments.

SUMMARY: The U.S. Environmental Protection Agency (EPA; Agency) is today issuing proposed guidelines for assessing the risks for neurotoxicity from exposure to environmental agents. As background information for this guidance, this notice describes the scientific basis for concern about exposure to agents that cause neurotoxicity and outlines the general process for assessing potential risk to humans because of environmental contaminants.

These proposed Guidelines for Neurotoxicity Risk Assessment (hereafter "Guidelines") are intended to guide Agency evaluation of agents that are suspected to cause neurotoxicity in line with the policies and procedures established in the statutes administered by the EPA. The Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Risk Assessment Forum, within EPA's Office of Research and Development. Draft Guidelines were developed by an Agency work group composed of scientists from throughout the Agency, and selected drafts were peer reviewed internally and by experts from universities, environmental groups, industry, and other governmental agencies. A subsequent draft has undergone peer review in a workshop held on June 2-3, 1992, and has received internal review by the Concordance and Oversight Subcommittees of the Risk Assessment Forum. Most recently, the Committee on the Environment and Natural Resources of the Office of Science and Technology Policy reviewed the guidelines at a meeting held on August 15, 1995. The proposed Guidelines are based, in part, on recommendations derived from these reviews and on those made at various scientific meetings and workshops on neurotoxicology.

The public is invited to comment, and public comments will be considered in EPA decisions in formulating the final Guidelines. Commenters are asked to focus on several special issues, particularly, (1) the issue of compensation and recovery of function

in neurotoxicological studies and how to account for compensation in neurotoxicology risk assessment; (2) the use of blood and/or brain acetylcholinesterase activity as an indication of neurotoxicity for risk assessment; (3) endpoints indicative of neurotoxicity that may not be covered by these guidelines, i.e., endocrine disruption or neuroendocrine-mediated neurotoxicity; and (4) the possibility of no threshold for some neurotoxic agents.

The EPA Science Advisory Board (SAB) also will review these proposed Guidelines at a meeting to be announced in a future Federal Register. Agency staff will prepare summaries of the public and SAB comments, analyses of major issues presented by commenters, and Agency responses to those comments. Appropriate comments will be incorporated, and the revised Guidelines will be submitted to the Risk Assessment Forum for review. The Agency will consider comments from the public, the SAB, and the Risk Assessment Forum in its recommendations to the EPA Administrator.

DATES: The Proposed Guidelines are being made available for a 120-day public review and comment period. Comments must be in writing and must be postmarked by February 1, 1996. Please submit one unbound original with pages consecutively numbered, and three copies. If there are attachments, include an index numbered consecutively with comments, and three copies.

FOR FURTHER INFORMATION CONTACT: Dr. Hugh A. Tilson, Tel: 919–541–2671; Fax: 919–541–4849.

ADDRESSES: Comments on the proposed Guidelines may be mailed or delivered to: Dr. Hugh A. Tilson, Neurotoxicology Division (MD–74B), National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711. Please note that all comments received in response to this notice will be placed in a public record. Commenters should not send any item of personal information, such as medical information or home address, if they do not wish it to be part of the public record.

SUPPLEMENTARY INFORMATION: In its 1983 book, Risk Assessment in the Federal Government: Managing the Process, the National Academy of Sciences recommended that Federal regulatory agencies establish "inference guidelines" (1) to promote consistency and technical quality in risk assessment, and (2) to ensure that the risk

assessment process is maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

In 1984, EPA scientists began work on risk assessment guidelines for carcinogenicity, mutagenicity, suspect developmental toxicants, chemical mixtures, and exposure assessment. Following extensive scientific and public review, these first five guidelines were issued on September 24, 1986 (51 FR 33992-34054). Since 1986, additional risk assessment guidelines have been proposed for male and female reproductive risk (53 FR 24834-847; 53 FR 24850-869), and two of the 1986 guidelines, suspect developmental toxicants (56 FR 63798-826) and exposure assessment (57 FR 22888-938), have been revised, reproposed, and finalized.

The Guidelines proposed today continue the guidelines development process initiated in 1984. These Guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments and to inform Agency decision makers and the public about these procedures. In particular, the Guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts study scientific information on each chemical under review and use the most scientifically appropriate interpretation to assess risk. The Guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

The Guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Dated: September 25, 1995. Carol M. Browner,

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Administrator.

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